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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,871	01/24/2002	James D. Thacker	38599.0012	5347

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/053,871	THACKER, JAMES D.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed March 3, 2004 has been entered. The examiner acknowledges the amendment to the specification. Claims 1-7,10,12-19,21,23,26,27,33 and 34 have been amended. Claims 36-44 have been newly added. Claims 1-44 are under consideration in this application.

Withdrawal of Objections and Rejections

2. The following objections and rejections have been withdrawn in view of applicants' amendments and arguments:

a) the objection of claim 27;

b) the written description rejection of claim 1-25 under 35 U.S.C. 112, first paragraph;

c) the scope of enablement rejection claims 1-35 under 35 U.S.C. 112, first paragraph;

Response to Arguments

3. Applicant's arguments filed March 3, 2004 have been fully considered but they are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The rejection of claims 1-25 and 36-39 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained. Applicant asserts that the amendments overcome the rejections. However it is the examiner's position that the amendments do not overcome all the rejections for the reasons stated below.

5. Claim 1 is unclear. Claim 1 recites adding a second antibody specific for said primary antibody and conjugated to a reporter molecule to the digested bacteria. It is unclear what the reporter is conjugated too (the first or second antibody) and how to interpret "conjugated to a reporter molecule to the digested bacteria." Claim 1 is also unclear with the recitation of "adding a primary antibody specific to said marker to the digested bacteria." It is understood that the primary antibody is specific to the marker, however it is unclear how to interpret "said marker to the digested bacteria" Is applicant saying that the primary antibody is specific to said marker digested by the bacteria? Therefore, clarification is required to overcome the rejection.

6. The addition steps in claims 1 and 13 recite adding primary and secondary antibody, however there are no contact steps. The claims refer to contacting a single primary antibody specific for the marker, however the claims fail to require contact between the primary antibody and the unidentified marker. It is still unclear where the antibodies are being added, i.e., the solid support or sample preparation or somewhere else.

7. It is unclear how determination of the type of bacteria can occur, see claims 1 and 13. Claims 1-44 recite detecting the bacteria based on the marker, there are no steps that recite detection based on the type of bacteria, therefore, it is unclear how typing of the bacteria can occur. Moreover, new claims 38-39 and 43-44 are unclear. Clarification is required to overcome the rejection. Moreover, the claims fail to recite the use of multiple antibodies specific for different types of microorganisms, thus it is unclear how the microorganisms can be typed. Furthermore, it is unclear how one could determine what type of microorganism is present in the sample unless one already knew what microorganisms were in the sample and what antibodies to use to detect such microorganisms. Yet the claims do not recite such steps. Thus, the claims are so unclear, that the metes and bounds cannot be ascertained. Clarification is required since applicants' assertions are not persuasive.

8. Claims 41- 42 are drawn to kit claims, however the claim recites a step for contacting the primary antibody. It is unclear how the kit claim can comprise a method step. Therefore, clarification is required to overcome the rejection and applicants' assertions are not persuasive.

9. Claims 1-25 and 36-39 are rejected as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MEP. § 2172.01. Despite applicants' arguments to the contrary the claims still lack essential contact steps and correlation steps that correlate the detected reporter molecule to determining

the type or quantity of microorganisms as previously discussed. Positive recitation of the essential method steps is required, and without such recitation there exist a gap between the steps.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Neither the specification nor originally presented claims provides support for immobilizing a capture antibody specific to one or more types of bacteria on a solid support. Applicant did not point to support in the specification for immobilizing a capture antibody specific to one or more types of bacteria on a solid support. Moreover, applicants failed to specifically point to the identity or provide structural characteristics of an immobilized capture antibody specific to one or more types of bacteria. Thus, there appears to be no teaching of an immobilized capture antibody specific to one or more types of bacteria. Applicant claims that there is support in instant specification and claims for support of the amendment which are drawn to an immobilized capture

antibody specific to one or more types of bacteria, however it appears that the entire specification appears to fail to recite support for the newly recited immobilized capture antibody specific to one or more types of bacteria. Rather the specification refers to methods useful for the detection of a single or mixed species of microorganisms using antibody specific to the marker. Therefore, it appears that there is no support in the specification. Therefore, applicants must specifically point to page and line number support for the identity an immobilized capture antibody specific to one or more types of bacteria as recited by the newly amended claims. Therefore, the new claims incorporate new matter and are accordingly rejected.

11. Claims 8, 25 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 8, 25 and 29 are drawn to reporter molecule is selected from the group consisting of bioluminescent protein, a chemiluminescent dye, fluorescent dye, an enzyme, latex particle, a magnetic particle, a radioisotope, a visible dye, and combinations thereof. The written description in this case only sets forth the specific reporters separately, however there is no written description of combinations of reporters, therefore the written description is not commensurate in scope with the claims drawn to combinations thereof. Neither the specification nor the claims teach how to use a combination of reporters in a single assay or kit. Neither the claims nor the

specification teach how to use a combination of reporter molecules in the claimed method or kit. There is no guidance as to what combinations of reporter molecules can be used together and which ones cannot be used in the assay or kit. The specification does not include structural examples of a combination of reporter molecules. Thus, the resulting combination of reporter molecules could result in a complex not taught and enabled by the specification.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of specifically named reporter molecules such as bioluminescent protein, a chemiluminescent dye, fluorescent dye, an enzyme, latex particle, a magnetic particle, a radioisotope, a visible dye, the skilled artisan cannot envision the detailed structure of a combination of reporter molecules thereof, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. Furthermore, *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of by only their functional activity does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every

species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus. Therefore only the recited reporter molecules (bioluminescent protein, a chemiluminescent dye, fluorescent dye, an enzyme, latex particle, a magnetic particle, a radioisotope, a visible dyes) and not the full breadth of the claims meet the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Thacker (WO 99/12015). The claims are drawn to a method for the typing or enumeration of bacteria comprising an immobilization step; two separate contacting steps; a digestion step; two addition steps; a detection step and a determination step. The dependant claims are drawn to the level of detection, time periods, reporter molecules, a variety of sample types and additional method steps.

Thacker teach methods for the rapid detection and enumeration of viable microorganisms. The methods can detect the presence of enzymes or detect the presence of metabolic activity (page 6). The viability substrate is metabolized by the microorganisms to a single water-insoluble marker molecule (page 7). This marker molecule or viability marker accumulates rapidly and in direct proportion to the number

of microorganisms present in the sample (page 7). The microorganisms are digested in a manner to produce cellular debris (page 7). Primary antibodies specific to the viability marker are added to the sample and affinity adsorbed to the surface of the cellular debris (page 7). It is noted that the primary antibodies can bind to one or more types of bacteria when the bacteria has digested the marker; therefore the primary antibodies can act as capture antibodies when immobilized to a surface. Secondary antibodies, specific for the primary antibodies can be conjugated to a reporter molecule like an enzyme, luminescent protein, radioisotope, fluorescent dye and the like (page 7). The reporter molecule is quantitatively detected either directly or indirectly after the addition of the appropriate activator or enzyme substrate (page 7). One method for amplifying the presence of an actively respiring microorganism in a sample is to contact the contents of the sample with a nutrient medium containing a predetermined amount of viability substrate wherein metabolism of the marker produces a viability marker (page 7). The preferable substrates include tetrazolium salts, triphenyltetrazolium, nitrotetrazolium blue, iodonitrotetrazolium or dimethyl thiazolyldiphenyl tetrazolium (page 8). The nutrient media should contain glucose and NADH (page 8). A variety of detection methods are taught. One method amplifies the microorganisms; contacts the primary antibody specific for the marker, and contacts a detectably labeled secondary antibody specific for the primary antibody to enable detection (page 8-9). One embodiment comprises the steps of amplifying the microorganisms utilizing microbial enzymatic conversions of tetrazolium salts to formazan products, capturing digested microbial cell fragments with immobilized primary antibodies specific to the formazan

and amplifying the presence of captured cell fragments with reporter antibodies prepared from primary antibodies conjugated to detectable markers. Another embodiment contacts the captured digested microorganism with a reporter antibody prepared from the primary antibody, the reporter antibody conjugated to a detectable marker and detecting the reporter antibody bound to the captured microorganism (page 9). Also the primary antibodies can be immobilized on a solid surface to (page 9). The method can also include an incubation step wherein the sample is incubated with a lysozyme to form cellular debris (page 9). The methods are useful in detection of a single species of microorganisms or a mixed population and can be used to reliably detect microorganisms in samples containing less than 1000 cfu/mL in less than 2 hours (page 11). Various sample types can be used with the method including clinical, food, cosmetic, pharmaceutical, industrial or environmental samples (page 11). Example 1 teaches a MicroDot assay, example 2 teaches an antigen capture ELISA, example 3 teaches a bioluminescence assay, and example 4 teaches chemilumescence assay. The examples teach the use of wash, dilution and digestion buffers and detection of one or more types of bacteria.

Therefore, Thacker teaches method for typing or enumerating bacteria in a sample comprising immobilizing capture antibody; contacting the sample with the immobilized antibody; allowing the production of the marker; digesting the marker; adding primary and secondary antibody; detecting the reporter molecule and determining the type or quantity of the bacteria in the sample just as instantly claimed.

The claims are also drawn to a kit comprising a soluble substrate; primary antibody and detectable reporter. The dependant kit claims are further drawn to additional buffers; reporter molecules, nutrient media; capture antibodies and secondary antibodies. Thacker also teaches kits for the rapid and sensitive detection and enumeration of viable microorganisms in a sample. The kits contain various components such as solid supports, chemical biomarkers such as tetrazolium salts, capture, primary and secondary antibodies, and detectable labels (page 10). The kits can contain all the components needed for a person to test a sample for the presence of viable microorganisms (page 10).

Moreover all the components recited in the kits are the same components discussed above as being useful to complete assays for rapid detection or enumeration of bacteria. Therefore, Thacker teaches kits for the detection or enumeration of one or more types of bacteria comprising the same components such as a soluble substrate (tetrazolium), primary antibodies specific for the marker; secondary antibodies, detectable reporter molecules, wash, dilution and digestions buffers, nutrient media just as recited by the instant claims.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
April 29, 2004

L. F. Smith
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